10. (Amended.) The method of Claim 8 where the pathologically proliferating cells are pathologically proliferating mammalian cells and the administering kills the pathologically proliferating mammalian cells or reduces the rate of proliferation of the pathologically proliferating cells by at least 10%.

Amend Claim 12 to be as follows:

12. (Amended.) The method of Claim 11 wherein the pathologically proliferating mammalian cells are those in Hodgkin's disease, in small cell lung cancer, in cancer of the breast, in testicular cancer or in prostate cancer.

**Remarks**

Claims 1-7 and 15-20 stand withdrawn from consideration after not being elected in response to a restriction requirement. Claims 1-7 and 15-20 are canceled herewith to advance the prosecution.

That leave Claims 8-14. All these claims have been examined.

Claims 9, 10 and 12 are amended herewith.

Claim 9 has been amended to connect the pathologic bacteria or fungus mentioned in the first part of the claim with the infection mentioned later in the claim.

Claims 9 and 10 have been amended to quantify the growth reduction. Basis for the amendment is submitted to be found in the application as filed at page 20, line 21-page 21, line 2.

Claim 12 has been amended herewith to correct an apparent typographical error.

A version with markings to show changes made is enclosed.

Claims 8-14 have not been rejected based on prior art.

Claims 8-14 have been rejected under 35 U.S.C. 112, first paragraph on the basis that the

specification does not provide enablement for killing or reducing the growth of pathologically proliferating mammalian cells. Gura, Science 278, 1041-1042 (11/97) is relied on for a statement that model systems (apparently animal model systems) are not predictive for drugs for cancer in humans. Reconsideration is requested.

Firstly, it is noted that Claim 9 is not addressed to treating pathologically proliferating mammalian cells. Thus, the rejection should not apply to Claim 9. Perhaps that is why it is indicated on the PTO-326, that Claim 9 is objected to.

Secondly, it is noted that Claim 12 names specific cancers. The specific cancer named are each the subject of a prophetic example. Perhaps this is why it is indicated in the PTO-326, that Claim 12 is objected to.

Thirdly, the citation of Gura is submitted to be misapplied. It is already known that manipulators of nitrosative stress (including NO donors) are useful to treat mammals for conditions associated with pathologically proliferating mammalian cell growth including cancer. See U.S. Patent No. 6,057,367, cited at page 1 of the instant patent application. The invention here relies on the discovery that a known enzyme has S-nitrosoglutathione reductase activity and therefore would mediate the proliferation of pathologically proliferating cells by interfering with nitrosative stress. The activity of the enzyme is shown at pages 32 and 33 to be present in three kinds of human cells leading to the conclusion that the activity is widespread in various human cell lines. Thus, applicant does not have to rely on animal models as derogated by Gura. In view of this, it is submitted that the rejection does not meet the standard of Ex parte Reese, 40 U.S.P.O. 2d 1221 (Bd App. 1996) which places the burden on the PTO of establishing a *prima facie* case of lack of enablement. See also In re Dinh, 181 U.S.P.Q. 46, 47 (C.C.P.A. 1974); In re Bowen,

181, U.S.P.Q. 48 (C.C.P.A. 1974) and In re Gardner, 177 U.S.P. 396,397 (C.C.P.A. 1973). Furthermore, consider that it is inappropriate for the PTO to take a position that *in vitro* and or animal tests are inherently incapable of supporting claims which embrace treating of human for cancer. See Ex parte Chwang, 231 U.S.P.Q. 751 (Bd. App. 1986).

Withdrawal of the rejection under 35 U.S.C. 112, first paragraph, is requested.

Claims 8-14 have been rejected under 35 U.S.C. 112, second paragraph, on a number bases. This is treated below.

Objection is made to the term "pathologically proliferating cells" in Claim 8. In response, it is noted that the term is defined at page 3, lines 13-14 of the instant patent application.

Objection is made to the term "pathologically proliferating cells" at Claim 9, line 1, Claim 10, line 1 and Claim 13, line 1. In response, it is noted that the term is defined in each of Claims 9, 10 and 13 as to what it means in each claim respectively.

Objection is made to the term "pathologic bacteria or fungus". In response, it is submitted that the term is defined in the application as filed at page 19, lines 16-20, which incorporates by reference columns 11 and 12 of U.S. Patent No. 6,057,367.

Objection is made to the term "bacterial or fungal infection" in Claim 9. In response, the claim is amended to connect the term with what is stated before.

Objection is made to the term "reduces the growth" at Claim 9, line 3 and Claim 10, line 2. In response, the term is quantified by amendment of Claims 9 and 10 herewith.

Objection is made to the term "pathologically proliferating mammalian cells" in Claim 10, line 3, Claim 11, line 1 and Claim 12, line 1. In response, it is noted that the term is defined in the application as filed at page 20, lines 10-18.

Objection is made to the term "small cell being cancer" in Claim 12. Correction is made by amendment of Claim 12 herewith.

Reconsideration of the rejection under 35 U.S.C. 112, second paragraph is requested.

Allowance is requested.

Respectfully submitted,

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Case Duke File No. 1838

Date: November 13, 2002

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

Claim 9 has been amended as follows:

9. (Amended.) The method of Claim 8 where the pathologically proliferating cells comprise pathologic bacteria or fungus and the patient is afflicted with a bacterial or fungal infection which is mediated or caused by the pathologic bacteria or fungus and the administering kills [or reduces the growth of] the pathologic bacteria or fungus or reduces the rate of proliferation of the pathologic bacteria or fungus by at least 10%.

Claim 10 has been amended as follows:

10. (Amended.) The method of Claim 8 where the pathologically proliferating cells are pathologically proliferating mammalian cells and the administering kills [or reduces the growth of] the pathologically proliferating mammalian cells or reduces the rate of proliferation of the pathologically proliferating cells by at least 10%.

Claim 12 has been amended as follows:

12. (Amended.) The method of Claim 11 wherein the pathologically proliferating mammalian cells are those in Hodgkin's disease, in small cell [being] lung cancer, in cancer of the breast, in testicular cancer or in prostate cancer.

Claims 1-7 and 15-20 have been canceled.